



## SEQUENCE LISTING

<110> OXVIG, Claus  
OVERGAARD, Michael T.

<120> PREGNANCY-ASSOCIATED PLASMA PROTEIN-A2 (PAPP-A2)

<130> OXVIG=1A

<140> US 09/983,025  
<141> 2001-10-22

<150> US 60/241,840  
<151> 2000-10-20

<150> DK PA 2000 01571  
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<170> PatentIn version 3.1

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9/12

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Gln Pro Gly Thr Trp Thr His Val Ala Ala Thr Tyr Asp Gly Arg His	
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Leu Gly Gly Asp Ser Ser Glu Asp Gly His Tyr Phe Arg Gly His Leu	
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Gly Thr Leu Val Phe Trp Ser Thr Ala Leu Pro Gln Ser His Phe Gln	

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Leu	Thr	Ala	Ser	Phe	Glu	Pro	Val	Asn	Thr	Glu	Trp	Val	Pro	Phe	Arg					
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Pro	Glu	Ile	Leu	Ser	Pro	Leu	Gln	Pro	Pro	Leu	Cys	Gly	Gln	Thr	Val					
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Cys	Asp	Asn	Val	Glu	Leu	Ile	Ser	Gln	Tyr	Asn	Gly	Tyr	Trp	Pro	Leu					
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Ser Thr His Phe Leu Asn Ile Tyr Phe Ala Ser Ser Val Arg Glu Asp	
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Pro Thr Pro Lys Ser Glu Leu Cys Arg Glu Pro Glu Pro Thr Ser Asp	
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aca gag atc ttg ctg gaa aac aag gag tca gtg cac ctg ggc ccc tta Thr Glu Ile Leu Leu Glu Asn Lys Glu Ser Val His Leu Gly Pro Leu	755	760	765	2997
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aag gtg tcg ggg gtg aaa gtc tac acc ttt gat gag agg ata gag att Lys Val Ser Gly Val Lys Val Tyr Thr Phe Asp Glu Arg Ile Glu Ile	785	790	795	3093
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ggt ttg ccc gtg gtg gtg aca cat tct cac agg aag ttc acg gac gtg Gly Leu Pro Val Val Val Thr His Ser His Arg Lys Phe Thr Asp Val	835	840	845	3237
gag gtc aca cct gga cag atg tat cag tac caa gtt cta gct gaa gct Glu Val Thr Pro Gly Gln Met Tyr Gln Tyr Gln Val Leu Ala Glu Ala	850	855	860	3285
gga gga gaa ctg gga gaa gct tcg cct cct ctg aac cac att cat gga Gly Gly Glu Leu Gly Glu Ala Ser Pro Pro Leu Asn His Ile His Gly	865	870	875	3333
gct cct tat tgt gga gat ggg aag gtg tca gag aga ctg gga gaa gag Ala Pro Tyr Cys Gly Asp Gly Lys Val Ser Glu Arg Leu Gly Glu Glu	880	885	890	3381

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gag ctg gag gaa ggt ttc aac tgt gta gga gag cca agc ctt tgc tac Glu Leu Glu Glu Gly Phe Asn Cys Val Gly Glu Pro Ser Leu Cys Tyr 915 920 925	3477
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gct acc cgg gct tac tcc tct cat gaa gac aag aag aag tgt cct gtt Ala Thr Arg Ala Tyr Ser Ser His Glu Asp Lys Lys Lys Cys Pro Val 960 965 970	3621
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Pro	Pro	Ala	Lys	Leu	Gln	Gly	Leu	Ser	Pro	Trp	Leu	Thr	Cys	Leu						
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1325								1330				1335								



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Val Arg Asn Lys	Leu Leu Lys Ile Gln	Cys Leu Glu Gly Gly Ile	
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Trp Glu Gln Gly	Ser Cys Ile Pro Val	Val Cys Glu Pro Pro Pro	
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Pro Val Phe Glu	Gly Met Tyr Glu Cys	Thr Asn Gly Phe Ser Leu	
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Asp Ser Gln Cys	Val Leu Asn Cys Asn	Gln Glu Arg Glu Lys Leu	
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Pro Ile Leu Cys	Thr Lys Glu Gly Leu	Trp Thr Gln Glu Phe Lys	
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ctg aat tct gtg	gag tac aaa tgt gaa	caa gga tat ggg att ggt	5022
Leu Asn Ser Val	Glu Tyr Lys Cys Glu	Gln Gly Tyr Gly Ile Gly	
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Ala Val Cys Ser	Pro Leu Cys Val Ile	Pro Pro Ser Asp Pro Val	
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Met Leu Pro Glu	Asn Ile Thr Ala Asp	Thr Leu Glu His Trp Met	
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gaa cct gtc aaa	gtc cag agc att gtg	tgc act ggc cgg cgt caa	5157
Glu Pro Val Lys	Val Gln Ser Ile Val	Cys Thr Gly Arg Arg Gln	
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Trp His Pro Asp	Pro Val Leu Val His	Cys Ile Gln Ser Cys Glu	
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ccc ttc caa gca	gat ggt tgg tgt gac	act atc aac aac cga gcc	5247
Pro Phe Gln Ala	Asp Gly Trp Cys Asp	Thr Ile Asn Asn Arg Ala	
1505	1510	1515	
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Tyr Cys His Tyr	Asp Gly Gly Asp Cys	Cys Ser Ser Thr Leu Ser	
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Ser Lys Lys Val	Ile Pro Phe Ala Ala	Asp Cys Asp Leu Asp Glu	
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Cys Thr Cys Arg	Asp Pro Lys Ala Glu	Glu Asn Gln	

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Thr Asp Arg Val Lys Lys Ala Thr Ile Leu Ile Ser His Ser Arg Tyr  
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His Gln Asn Val Leu Phe His His Thr Thr Ser Val Leu Leu Asn  
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<210> 19

<211> 10

<212> PRT

<213> Artificial Sequence

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<400> 19

Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu

1

5

10

<210> 20

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> synthetic linker in pPA2-mH

<400> 20

Asn Ser Ala Val Asp

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5

<210> 21

<211> 30

<212> DNA

<213> Artificial Sequence

<220>

<223> primer containing XhoI site, for amplifying IGFBP-5 cDNA

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30

<210> 22

<211> 29

<212> DNA

<213> Artificial Sequence

<220>

<223> primer containing HindIII site, for amplifying IGFBP-5 cDNA

<400> 22

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29



<210> 23  
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 <212> PRT  
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 <223> N-terminal sequence of degradation product of purified rIGFBP-5  
 digested with PAPP-A2

<400> 23

Lys Phe Val Gly Gly Ala  
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<210> 24  
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 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> N-terminal sequence of degradation product of purified rIGFBP-5  
 digested with PAPP-A2

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 <221> misc\_feature  
 <222> (3)..(3)  
 <223> Xaa is unknown

<400> 24

Leu Gly Xaa Phe Val His  
 1 5

<210> 25  
 <211> 1627  
 <212> PRT  
 <213> Homo sapiens

<400> 25

Met Arg Leu Trp Ser Trp Val Leu His Leu Gly Leu Leu Ser Ala Ala  
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Leu Gly Cys Gly Leu Ala Glu Arg Pro Arg Arg Ala Arg Arg Asp Pro  
 20 25 30

Arg Ala Gly Arg Pro Pro Arg Pro Ala Ala Gly Pro Ala Thr Cys Ala  
 35 40 45

Thr Arg Gly Pro Arg Pro Pro Arg Leu Ala Ala Ala Ala Ala Ala  
 50 55 60

Gly Arg Ala Trp Glu Ala Val Arg Val Pro Arg Arg Arg Gln Gln Arg  
65 70 75 80

Glu Ala Arg Gly Ala Thr Glu Glu Pro Ser Pro Pro Ser Arg Ala Leu  
85 90 95

Tyr Phe Ser Gly Arg Gly Glu Gln Leu Arg Val Leu Arg Ala Asp Leu  
100 105 110

Glu Leu Pro Arg Asp Ala Phe Thr Leu Gln Val Trp Leu Arg Ala Glu  
115 120 125

Gly Gly Gln Arg Ser Pro Ala Val Ile Thr Gly Leu Tyr Asp Lys Cys  
130 135 140

Ser Tyr Ile Ser Arg Asp Arg Gly Trp Val Val Gly Ile His Thr Ile  
145 150 155 160

Ser Asp Gln Asp Asn Lys Asp Pro Arg Tyr Phe Phe Ser Leu Lys Thr  
165 170 175

Asp Arg Ala Arg Gln Val Thr Thr Ile Asn Ala His Arg Ser Tyr Leu  
180 185 190

Pro Gly Gln Trp Val Tyr Leu Ala Ala Thr Tyr Asp Gly Gln Phe Met  
195 200 205

Lys Leu Tyr Val Asn Gly Ala Gln Val Ala Thr Ser Gly Glu Gln Val  
210 215 220

Gly Gly Ile Phe Ser Pro Leu Thr Gln Lys Cys Lys Val Leu Met Leu  
225 230 235 240

Gly Gly Ser Ala Leu Asn His Asn Tyr Arg Gly Tyr Ile Glu His Phe  
245 250 255

Ser Leu Trp Lys Val Ala Arg Thr Gln Arg Glu Ile Leu Ser Asp Met  
260 265 270

Glu Thr His Gly Ala His Thr Ala Leu Pro Gln Leu Leu Leu Gln Glu  
275 280 285

Asn Trp Asp Asn Val Lys His Ala Trp Ser Pro Met Lys Asp Gly Ser

290					295					300					
Ser	Pro	Lys	Val	Glu	Phe	Ser	Asn	Ala	His	Gly	Phe	Leu	Leu	Asp	Thr
305					310					315					320
Ser	Leu	Glu	Pro	Pro	Leu	Cys	Gly	Gln	Thr	Leu	Cys	Asp	Asn	Thr	Glu
				325					330					335	
Val	Ile	Ala	Ser	Tyr	Asn	Gln	Leu	Ser	Ser	Phe	Arg	Gln	Pro	Lys	Val
			340					345					350		
Val	Arg	Tyr	Arg	Val	Val	Asn	Leu	Tyr	Glu	Asp	Asp	His	Lys	Asn	Pro
		355					360					365			
Thr	Val	Thr	Arg	Glu	Gln	Val	Asp	Phe	Gln	His	His	Gln	Leu	Ala	Glu
	370					375					380				
Ala	Phe	Lys	Gln	Tyr	Asn	Ile	Ser	Trp	Glu	Leu	Asp	Val	Leu	Glu	Val
385					390					395					400
Ser	Asn	Ser	Ser	Leu	Arg	Arg	Arg	Leu	Ile	Leu	Ala	Asn	Cys	Asp	Ile
				405					410					415	
Ser	Lys	Ile	Gly	Asp	Glu	Asn	Cys	Asp	Pro	Glu	Cys	Asn	His	Thr	Leu
			420					425					430		
Thr	Gly	His	Asp	Gly	Gly	Asp	Cys	Arg	His	Leu	Arg	His	Pro	Ala	Phe
	435						440					445			
Val	Lys	Lys	Gln	His	Asn	Gly	Val	Cys	Asp	Met	Asp	Cys	Asn	Tyr	Glu
	450					455					460				
Arg	Phe	Asn	Phe	Asp	Gly	Gly	Glu	Cys	Cys	Asp	Pro	Glu	Ile	Thr	Asn
465					470					475					480
Val	Thr	Gln	Thr	Cys	Phe	Asp	Pro	Asp	Ser	Pro	His	Arg	Ala	Tyr	Leu
				485					490					495	
Asp	Val	Asn	Glu	Leu	Lys	Asn	Ile	Leu	Lys	Leu	Asp	Gly	Ser	Thr	His
			500					505					510		
Leu	Asn	Ile	Phe	Phe	Ala	Lys	Ser	Ser	Glu	Glu	Glu	Leu	Ala	Gly	Val
		515					520					525			

Ala Thr Trp Pro Trp Asp Lys Glu Ala Leu Met His Leu Gly Gly Ile  
 530 535 540

Val Leu Asn Pro Ser Phe Tyr Gly Met Pro Gly His Thr His Thr Met  
 545 550 555 560

Ile His Glu Ile Gly His Ser Leu Gly Leu Tyr His Val Phe Arg Gly  
 565 570 575

Ile Ser Glu Ile Gln Ser Cys Ser Asp Pro Cys Met Glu Thr Glu Pro  
 580 585 590

Ser Phe Glu Thr Gly Asp Leu Cys Asn Asp Thr Asn Pro Ala Pro Lys  
 595 600 605

His Lys Ser Cys Gly Asp Pro Gly Pro Gly Asn Asp Thr Cys Gly Phe  
 610 615 620

His Ser Phe Phe Asn Thr Pro Tyr Asn Asn Phe Met Ser Tyr Ala Asp  
 625 630 635 640

Asp Asp Cys Thr Asp Ser Phe Thr Pro Asn Gln Val Ala Arg Met His  
 645 650 655

Cys Tyr Leu Asp Leu Val Tyr Gln Gly Trp Gln Pro Ser Arg Lys Pro  
 660 665 670

Ala Pro Val Ala Leu Ala Pro Gln Val Leu Gly His Thr Thr Asp Ser  
 675 680 685

Val Thr Leu Glu Trp Phe Pro Pro Ile Asp Gly His Phe Phe Glu Arg  
 690 695 700

Glu Leu Gly Ser Ala Cys His Leu Cys Leu Glu Gly Arg Ile Leu Val  
 705 710 715 720

Gln Tyr Ala Ser Asn Ala Ser Ser Pro Met Pro Cys Ser Pro Ser Gly  
 725 730 735

His Trp Ser Pro Arg Glu Ala Glu Gly His Pro Asp Val Glu Gln Pro  
 740 745 750

Cys Lys Ser Ser Val Arg Thr Trp Ser Pro Asn Ser Ala Val Asn Pro

755

760

765

His Thr Val Pro Pro Ala Cys Pro Glu Pro Gln Gly Cys Tyr Leu Glu  
 770 775 780

Leu Glu Phe Leu Tyr Pro Leu Val Pro Glu Ser Leu Thr Ile Trp Val  
 785 790 795 800

Thr Phe Val Ser Thr Asp Trp Asp Ser Ser Gly Ala Val Asn Asp Ile  
 805 810 815

Lys Leu Leu Ala Val Ser Gly Lys Asn Ile Ser Leu Gly Pro Gln Asn  
 820 825 830

Val Phe Cys Asp Val Pro Leu Thr Ile Arg Leu Trp Asp Val Gly Glu  
 835 840 845

----- Glu Val Tyr Gly Ile Gln Ile Tyr Thr Leu Asp Glu His Leu Glu Ile  
 850 855 860

Asp Ala Ala Met Leu Thr Ser Thr Ala Asp Thr Pro Leu Cys Leu Gln  
 865 870 875 880

Cys Lys Pro Leu Lys Tyr Lys Val Val Arg Asp Pro Pro Leu Gln Met  
 885 890 895

Asp Val Ala Ser Ile Leu His Leu Asn Arg Lys Phe Val Asp Met Asp  
 900 905 910

Leu Asn Leu Gly Ser Val Tyr Gln Tyr Trp Val Ile Thr Ile Ser Gly  
 915 920 925

Thr Glu Glu Ser Glu Pro Ser Pro Ala Val Thr Tyr Ile His Gly Arg  
 930 935 940

Gly Tyr Cys Gly Asp Gly Ile Ile Gln Lys Asp Gln Gly Glu Gln Cys  
 945 950 955 960

Asp Asp Met Asn Lys Ile Asn Gly Asp Gly Cys Ser Leu Phe Cys Arg  
 965 970 975

Gln Glu Val Ser Phe Asn Cys Ile Asp Glu Pro Ser Arg Cys Tyr Phe  
 980 985 990

His Asp Gly Asp Gly Val Cys Glu Glu Phe Glu Gln Lys Thr Ser Ile  
 995 1000 1005

Lys Asp Cys Gly Val Tyr Thr Pro Gln Gly Phe Leu Asp Gln Trp  
 1010 1015 1020

Ala Ser Asn Ala Ser Val Ser His Gln Asp Gln Gln Cys Pro Gly  
 1025 1030 1035

Trp Val Ile Ile Gly Gln Pro Ala Ala Ser Gln Val Cys Arg Thr  
 1040 1045 1050

Lys Val Ile Asp Leu Ser Glu Gly Ile Ser Gln His Ala Trp Tyr  
 1055 1060 1065

Pro Cys Thr Ile Ser Tyr Pro Tyr Ser Gln Leu Ala Gln Thr Thr  
 1070 1075 1080

Phe Trp Leu Arg Ala Tyr Phe Ser Gln Pro Met Val Ala Ala Ala  
 1085 1090 1095

Val Ile Val His Leu Val Thr Asp Gly Thr Tyr Tyr Gly Asp Gln  
 1100 1105 1110

Lys Gln Glu Thr Ile Ser Val Gln Leu Leu Asp Thr Lys Asp Gln  
 1115 1120 1125

Ser His Asp Leu Gly Leu His Val Leu Ser Cys Arg Asn Asn Pro  
 1130 1135 1140

Leu Ile Ile Pro Val Val His Asp Leu Ser Gln Pro Phe Tyr His  
 1145 1150 1155

Ser Gln Ala Val Arg Val Ser Phe Ser Ser Pro Leu Val Ala Ile  
 1160 1165 1170

Ser Gly Val Ala Leu Arg Ser Phe Asp Asn Phe Asp Pro Val Thr  
 1175 1180 1185

Leu Ser Ser Cys Gln Arg Gly Glu Thr Tyr Ser Pro Ala Glu Gln  
 1190 1195 1200

Ser Cys Val His Phe Ala Cys Glu Lys Thr Asp Cys Pro Glu Leu

1205		1210		1215
Ala Val Glu Asn Ala Ser Leu Asn Cys Ser Ser Ser Asp Arg Tyr				
1220		1225		1230
His Gly Ala Gln Cys Thr Val Ser Cys Arg Thr Gly Tyr Val Leu				
1235		1240		1245
Gln Ile Arg Arg Asp Asp Glu Leu Ile Lys Ser Gln Thr Gly Pro				
1250		1255		1260
Ser Val Thr Val Thr Cys Thr Glu Gly Lys Trp Asn Lys Gln Val				
1265		1270		1275
Ala Cys Glu Pro Val Asp Cys Ser Ile Pro Asp His His Gln Val				
1280		1285		1290
Tyr Ala Ala Ser Phe Ser Cys Pro Glu Gly Thr Thr Phe Gly Ser				
1295		1300		1305
Gln Cys Ser Phe Gln Cys Arg His Pro Ala Gln Leu Lys Gly Asn				
1310		1315		1320
Asn Ser Leu Leu Thr Cys Met Glu Asp Gly Leu Trp Ser Phe Pro				
1325		1330		1335
Glu Ala Leu Cys Glu Leu Met Cys Leu Ala Pro Pro Pro Val Pro				
1340		1345		1350
Asn Ala Asp Leu Gln Thr Ala Arg Cys Arg Glu Asn Lys His Lys				
1355		1360		1365
Val Gly Ser Phe Cys Lys Tyr Lys Cys Lys Pro Gly Tyr His Val				
1370		1375		1380
Pro Gly Ser Ser Arg Lys Ser Lys Lys Arg Ala Phe Lys Thr Gln				
1385		1390		1395
Cys Thr Gln Asp Gly Ser Trp Gln Glu Gly Ala Cys Val Pro Val				
1400		1405		1410
Thr Cys Asp Pro Pro Pro Pro Lys Phe His Gly Leu Tyr Gln Cys				
1415		1420		1425

Thr Asn Gly Phe Gln Phe Asn Ser Glu Cys Arg Ile Lys Cys Glu  
1430 1435 1440

Asp Ser Asp Ala Ser Gln Gly Leu Gly Ser Asn Val Ile His Cys  
1445 1450 1455

Arg Lys Asp Gly Thr Trp Asn Gly Ser Phe His Val Cys Gln Glu  
1460 1465 1470

Met Gln Gly Gln Cys Ser Val Pro Asn Glu Leu Asn Ser Asn Leu  
1475 1480 1485

Lys Leu Gln Cys Pro Asp Gly Tyr Ala Ile Gly Ser Glu Cys Ala  
1490 1495 1500

Thr Ser Cys Leu Asp His Asn Ser Glu Ser Ile Ile Leu Pro Met  
1505 1510 1515

Asn Val Thr Val Arg Asp Ile Pro His Trp Leu Asn Pro Thr Arg  
1520 1525 1530

Val Glu Arg Val Val Cys Thr Ala Gly Leu Lys Trp Tyr Pro His  
1535 1540 1545

Pro Ala Leu Ile His Cys Val Lys Gly Cys Glu Pro Phe Met Gly  
1550 1555 1560

Asp Asn Tyr Cys Asp Ala Ile Asn Asn Arg Ala Phe Cys Asn Tyr  
1565 1570 1575

Asp Gly Gly Asp Cys Cys Thr Ser Thr Val Lys Thr Lys Lys Val  
1580 1585 1590

Thr Pro Phe Pro Met Ser Cys Asp Leu Gln Gly Asp Cys Ala Cys  
1595 1600 1605

Arg Asp Pro Gln Ala Gln Glu His Ser Arg Lys Asp Leu Arg Gly  
1610 1615 1620

Tyr Ser His Gly  
1625